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EXAMINER	
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ART UNIT	PAPER NUMBER
1646	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/995,542	SHUTTER ET AL.	
	Examiner	Art Unit	
	Nirmal S. Basi	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 November 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-58* is/are pending in the application.

4a) Of the above claim(s) *1-8,10-12,18-37,44-46 and 48-58* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *9, 13-1,38-43,47-48* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Amendment filed 11/30/05 has been entered.

2. Claims 1-8, 10-12, 18-37, 44-46, 49-58 are withdrawn as non-elected inventions. Claims 9, 13-17, 38-43 and 47-48 are examined below.

Objection to the claims

3. Claim 40 contains non-elected invention, SEQ ID NO:3. The claim must be amended to remove non-elected invention.

Claim Rejections - 35 USC 101

4. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter or any new and useful improvement thereof, may obtain a patent therefore, subject to the conditions and requirements of this title.

Claims 9 is rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter.

The preamble of claim 9 recites "A polypeptide produced by a process" and the body of the claim recites "optionally isolating the polypeptide". The claim does not recite which specific polypeptide is produced and reads on every polypeptide known to man. The process does not limit which polypeptide is produced and since the polypeptide is not purified or isolated the claim as currently recited encompass these naturally occurring polypeptides. Therefore, the compounds as claimed are a product that occurs in nature and does not show the hand of man, and as such is non-statutory subject matter. It is

suggested that the claims be amended to recite an isolated and purified polypeptide to overcome this rejection.

Claim Rejections - 35 USC § 112, second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 9, 13-17, 38-43, 47 and 48 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 9 is indefinite because it is not clear from the preamble which polypeptide is being produced or isolated. If in fact Applicant is claiming every polypeptide known to man then the method steps do not achieve the goal of the claim. Claim 9 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: suitable conditions to express the polypeptide and the method of isolation of the polypeptide.

Claims 9 and 16 are indefinite because it is not clear when a fragment of the amino acid sequence set forth in SEQ ID NO:5 comprises "at least about 25 amino acid residues" or "at least about 16 amino acid residues" so as to allow the metes and bounds of the claim to be determined. When is a amino acid sequence "at least about 25 amino acid residues" as compared to not to at least about "at least about 25 amino acid residues" so as to allow the metes and

bounds of the claim to be determined. When is a amino acid sequence "at least about 16 amino acid residues" as compared to not to at least about "at least about 16 amino acid residues" so as to allow the metes and bounds of the claim to be determined. It is suggested the word "about" be removed to overcome the rejection. Further it is not clear which fragments would contain the claimed activity since the activity is not disclosed (see above). What is the activity of the polypeptide fragment?

Claims 9 and 16 are indefinite because the "moderately stringent hybridization" conditions are not specified. The metes and bounds of the group of sequences that would meet the limitations of the claim depend upon the precise conditions under which hybridizations were performed including wash conditions. Since the hybridization and wash conditions dictate which nucleic acid sequences remain specifically bound to the claimed polynucleotide the metes and bounds of the claim cannot be determined without the disclosure of said conditions.

Claim 14 remains indefinite because it is not clear which amino acid sequences are orthologs of SEQ ID NO:5. Applicant specification states that an ABCL ortholog is a polypeptide sequence from another species that corresponds to the ABCL sequence disclosed in, for example, SEQ ID NO:5. Applicant's arguments have been fully considered but are not found persuasive. It is not clear what sequences from another species that corresponds to the ABCL sequence disclosed in SEQ ID NO:5. What sequences are conserved for a polypeptide to be considered an ortholog of the polypeptide of SEQ ID NO:5? It

is not clear what structural and functional features of the polypeptide of SEQ ID NO:5 must be retained in a polypeptide that corresponds to the polypeptide of SEQ ID NO:5 for it to be considered an ortholog. The "corresponding" features are not disclosed so as to allow the metes and bounds of the claim to be determined.

Claims 9, 14, 15 and 16 are indefinite because it is not what activity the claimed polypeptide possesses and what activity is contained in the polypeptide of SEQ ID NO:5 so as to allow the metes and bounds of the claim to be determined. Applicants argue the specification provides ample description regarding the activity of the claimed ABCL polypeptide and the ABC transporter family of polypeptides. Applicants argue "for example, at pages 89-90 (Example 3), Applicants provide mRNA expression levels in human, monkey, and mouse tissue. The specification also teaches, for example at pages 76, line 28 to page 78, line 12, that ABCL polypeptides may be involved in transport of lipids, including cholesterol; neurosteroids, including DHEA and progesterone, development of thymus, spleen, thyroid, hypothalamus, and ganglia. Thus, the specification provides ample guidance and clarity regarding the activity/function of the claimed polypeptide to one of skill in the art." Applicant's arguments have been fully considered but are not found persuasive. The expression mRNA level is not an activity of the polypeptide claimed. mRNA is a polynucleotide and discloses nothing about the activity of the polypeptide which is made up of amino acids. Although it may be true that ABCL polypeptides may be involved in transport of lipids, including cholesterol; neurosteroids, including DHEA and

progesterone, development of thymus, spleen, thyroid, hypothalamus, and ganglia, the question is what is the activity of the claimed polypeptide. As indicated in the last office action all ABCL polypeptides do not have the same activity. It is still not clear from Applicants response what is the activity of the polypeptide set forth in SEQ ID NO:5. The question more specifically is not what activity the ABCL polypeptides have but what activity does the specifically claimed polypeptide set forth in SEQ ID NO:5 have. It is clear from the prior art and the specification that the claimed polypeptide does not have all the activities of all the known ABCL polypeptides. If examiners assessment is wrong and the claimed ABCL polypeptide is some "super ABLC transporter" with all the activities of all the ABCL transporters then it should be clearly indicated as such.

Claim 9, 14 and 16 are indefinite because the phrase allelic variant is not clearly defined so as to allow the metes and bounds of the claim be determined. Applicants argue the specification provides a clear and concise definition for the term "variant". Applicants argue, "From the teaching in the specification, one of skill clearly understands that variants can have from 1-3, 1-5, 1-10, 1-15, 1-20, 1-25, 1-50, 1-75, 1-100 or more than 100 amino acid modifications. Applicants have explicitly detailed a variant of SEQ ID N0: 5 by disclosing the sequence of SEQ ID N0: 6". Applicant's arguments have been fully considered but are not persuasive. The gene or allele encoding the polypeptide of SEQ ID NO:5 is not disclosed. The gene or allele for the variant polypeptide of SEQ ID NO:6 is not disclosed. The disclosed cDNA encoding the polypeptide of SEQ ID NO:5 is not a gene or allele. A gene or allele contains both introns and exons. The

intron/exon structure is not disclosed for the allele encoding the polypeptide of SEQ ID NO:5. Therefore if the structure of the allele is not known then the structure of the variants can also not be determined so as to allow the metes and bounds of the claim to be determined. The term variant carries no weight in terms of structure and function and encompasses an unlimited number of alterations and reads on unrelated molecules, especially as the applicant points out the variant can have more than 100 amino acid modifications. Therefore without the disclosure of the allele/gene encoding the polypeptide of SEQ ID NO:5 the metes and bounds of allelic variants and splice variants cannot be determined. There is no disclosure of the intron/exon structure of the gene encoding the polypeptide of SEQ ID NO:5. The specification does not disclose any allelic variants or splice variants.

Claim 9, 15, and 16 are indefinite because it is not clear which amino acid residues in the amino acid sequence of SEQ ID NO:5, when changed, are considered "conservative substitutions" and the polypeptide retains an undisclosed activity, so as to allow the metes and bounds of the claim to be determined. Applicants argue "the specification provides ample guidance to one of skill in the art such that he or she has clear and definite knowledge of the activity of the claimed polypeptide (see argument and citation to specification above). Further a detailed discussion regarding conservative amino acid substitutions is contained in the specification at, for example, page 19, line 18 to page 24, line 21. In particular, Applicants provide guidance for one of skill in determining suitable variants (including conservative amino acid substitutions),

for example, at page 22, line 3 to page 24, line 16. In light of all this guidance provided by the specification, one of skill in the art would have a clear understanding of the term conservative substitutions and the relationship to biological activity of the claimed polypeptides." Applicant's arguments have been fully considered but are not found persuasive. Applicants answer nor the specification provide any clear answers which amino acid substitutions in the polypeptide of SEQ ID NO:5 are considered conservative amino acid substitutions, which when made would give the polypeptide the activity of the polypeptide set forth in SEQ UID NO:5. Contrary to applicant's arguments neither the activity nor the conservative substitutions that allow the activity can be determined. The specification, page 19 and 20 discloses examples of "conservative substitutions". Neither the functional activity nor the biological activity of the claimed polypeptide is disclosed. The amino acid residues that are essential for the functional activity or the biological activity of the claimed polypeptide are not disclosed. Without a disclosure of which specific amino acids are considered "conservative substitutions", the metes and bounds of the claim to be determined. There is no disclosure of the critical feature of the invention that is required for its functionality/activity. Therefore, without knowledge of which one or more amino acids can be changed without affecting the undisclosed activity of the polypeptide disclosed in SEQ ID NO:5 the metes and bounds of the claim cannot be determined.

Claim 9, 15, and 16 are indefinite because it is not clear which amino acid residue insertion into the amino acid sequence of SEQ ID NO:5, produces a

polypeptide with the activity of the polypeptide of SEQ ID NO:5, so as to allow the metes and bounds of the claim to be determined. The amino acid residues that are essential for the functional activity or the biological activity of the claimed polypeptide are not disclosed. There is no disclosure of the critical feature of the invention that is required for its functionality/activity. Therefore, without knowledge of which amino acid can be changed without affecting the undisclosed activity of the polypeptide disclosed in SEQ ID NO:5 the metes and bounds of the claim cannot be determined.

Claim 9, 15 and 16, are indefinite because it is not clear which amino acid residue deletion into the amino acid sequence of SEQ ID NO:5, produces a polypeptide with the activity of the polypeptide of SEQ ID NO:5, so as to allow the metes and bounds of the claim to be determined. The amino acid residues that are essential for the functional activity or the biological activity of the claimed polypeptide are not disclosed. There is no disclosure of the critical feature of the invention that is required for its functionality/activity. Therefore, without knowledge of which amino acid can be changed without affecting the undisclosed activity of the polypeptide disclosed in SEQ ID NO:5 the metes and bounds of the claim cannot be determined.

Claim 9, 15, and 16 are indefinite because it is not clear which modification of specific amino acid residues of the amino acid sequence of SEQ ID NO:5 produces a polypeptide with the activity of the polypeptide of SEQ ID NO:5, so as to allow the metes and bounds of the claim to be determined. The activity is not disclosed. The amino acid residues that are essential for the

functional activity or the biological activity of the claimed polypeptide are not disclosed. There is no disclosure of the critical feature of the invention that is required for its functionality/activity. Therefore, without knowledge of which amino acid can be changed without affecting the undisclosed activity of the polypeptide disclosed in SEQ ID NO:5 the metes and bounds of the claim cannot be determined.

Claim 41 is indefinite because the term "derivative" is indefinite because it provides no information about the structure or function of the claimed polypeptide and encompasses an infinite number of possibilities.

Claims 13, 17, 38, 39, 40, 42, 43, 47 and 48 are rejected for depending on an indefinite base claim.

6.

Objection to the claims

Claim 40 contains non-elected invention. Reference to the non-elected Invention must be removed.

7. ***Claim Rejections - 35 USC 101 and 35 USC . 112, 1st paragraph***

The following is a quotation of 35 U.S.C. 101:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 9, 13-17, 38-43, 47 and 48 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility.

A specific utility is a utility that is specific to the subject matter claimed, as opposed to a general utility that would be applicable to the broad class of the invention. A "substantial utility" is a utility that defines a "real world" use. Utilities that require or constitute carrying out further research to identify or reasonably confirm a "real world" context of use are not substantial utilities. A "well established utility" is a utility that is well known, immediately apparent, or implied by the specifications disclosure of the properties of a material, alone or taken with the knowledge of one skilled in the art. A well established utility must also be specific and substantial as well as credible.

Applicant argue they provide a specific benefit to the public (i.e. particular member of the ABC transporter superfamily) and have asserted that the claimed polypeptides, can be used to treat, diagnose, ameliorate, or prevent a number of diseases, disorders, or conditions associated with ABC transporter polypeptides, for example using the claimed polypeptides to diagnose or treat diseases and conditions involving the thymus and spleen (e.g., lymphoid and myeloid cells

such as conditions including, for example, modulation of immune responses, aids, lymphomas, Leukemia's, neutropenia, anemia, and autoimmune diseases; thyroid (e.g., hypo- and hyperthyroidism; hypothalamus (e.g., obesity, diabetes, reproductive disorders, and energy balance disorders and ganglia (e.g., neuropathies including, Charcot-Marie-Tooth disease, Dejerine-Sottas syndrome, Guillain-Barr syndrome, diabetic neuropathy, and multiple sclerosis). Specification at pp. 77-78. Applicant's arguments have been fully considered but are not found persuasive. Applicant has provided no nexus between treating or diagnosing any one of the diseases listed above, let alone being able to treat them all. The activity of the claimed polypeptide as it relates to a specific function has not been disclosed.

Based on the record, there is not a "well established utility" for the claimed invention. Applicant has asserted utilities for the specifically claimed invention of claims 9, 13-17, 38-43, 47 and 48. The invention is directed to an isolated ABCL polypeptide comprising the amino acid sequence set forth in SEQ ID NO:5 and SEQ ID NO:6, variants and derivatives thereof. SEQ ID NO:5 has and additional 46 amino acid residues at the N-terminus as compared to SEQ ID NO:6.

The specification discloses the ABC transporter (ABCL) polypeptide (SEQ ID NO:5 and 6). The specification discloses that a variety of ABC transporters have been identified, and discloses that several ABC transporters have been implicated in the pathogenesis of disease (page 2). The specification further discloses an extensive list of disorders that may be associated ABC transporter dysfunction (page76-78) Members of the ATP-Binding Cassette (ABC)

transporter family are also highly divergent in their effects and ligand specificity. The outcome of the cellular signaling effect varies depending on the specific ABC transporter and the substrate transported. There is no experimental data provided as to the specific functionality of the claimed ABCL. There is no disclosure of the specific ligands that activate or bind it. There is no disclosure of the specific compound transported by claimed ABCL. Based on the homology data to ABC transporters ((ABCL has 54% and 49% amino acid sequence identity with ABC1 and ABCR, respectively, page 85) and a general classification into the superfamily of ABC transporters, the specification discloses that the claimed ABCL is useful for a variety of applications; including research, diagnostic, and therapeutic agent screening applications and treatment therapies. There is no clear nexus between any treatable diseases/disorders and use of claimed ABCL. There is no disclosure of the specific activity of the claimed ABC transporter or how to assay for said activity. In light of the specification, the skilled artisan cannot come to any conclusions as to the function of claimed ATP-Binding Cassette (ABC) transporter of SEQ ID NO:5 and 6.

The diversity in ABC transporter function and substrate specificity is disclosed in the specification page 2. The specification states, "The ATP-Binding Cassette (ABC) Transporter superfamily constitutes a large and diverse group of proteins that selectively mediate the movement of molecules across biological membranes. Over 100 ABC transporters have been identified, with the majority of these transporters being prokaryotic proteins. Although most members of this

superfamily have some specificity for a particular substrate or group of related substrates, the number and types of substrates transported by the different members of the superfamily varies widely. For example, ABC transporters having substrate-specificity for proteins, sugars, peptides, polysaccharides, amino acids, and inorganic ions have been identified. Furthermore, some ABC transporters function to import substrates while other ABC transporters function to export substrates". The substrate-specificity for ABCL is unknown. Also, not known if it imports or exports substrate. Further, not known is if ABCL normal or dysfunctional.

The utility of the claimed protein cannot be implicated solely from the homology to the proteins known in the art because the art does not provide a teaching stating that all protein disclosed have the same activity, the same effects, the same ligands and or are involved in the same disease states. In light of the teaching of the specification and art, the skilled artisan cannot come to any conclusions as to the function of the claimed polypeptide. There is no disclosure provided within the instant specification as to what specific function the proteins of SEQ ID NO:5 and 6 possesses or how to specifically assay for such function. There are no ligands that bind the protein or promoters that activate it. Additionally, there are no target cell types/tissues disclosed and no disease states disclosed that are directly related to protein dysfunction.

The specification fails to disclose what disease is associated with the claimed ABC transporter dysfunction or what drugs affect the specifically claimed ABC transporter function. None of the claims, specification, or prior art disclose

the ligand that binds claimed ABC transporter, the activity associated with claimed ABC transporter, how the activity is modulated, or how the modulation or activity is determined using specific assay steps. The claimed ABC transporter may have utility in the future, when it has been further characterized (e.g. its dysfunction or function correlated with a disease state) and its ligand or functionality determined. The inclusion in the family of ABC transporters does not constitute either a specific and substantial asserted utility or a well established utility for the claimed ABCL protein. This is analogous to the reasoning that all proteins/nucleic acid of ABC transporter proteins can be used as markers on a gel.

The specification discloses that the claimed ABC transporters are useful in screening but does not disclose what the claimed ABC transporters specifically regulate or what specific disease the claimed ABC transporter is a target for. What would be the use of using the claimed ABC transporter in a panel for drug screening? It has no known ligand or known function and so is an "orphan". How would one use compounds that interact with said orphan ABC transporter? The specification provides a diverse list of disease states that may be involved in ABC transporter dysfunction. It is unpredictable what ligands would bind or be transported by ABCL and what the result of such binding or transport would be. Further, the functional effects of ligand binding and compound transport may remain uncertain even after extensive experimentation. What is the utility for a ligand having no known function, that binds to an ABCL of no known function? The ordinary artisan can only speculate as to the utility for the ligand and ABCL.

No utility to orphan ABCL can be assigned without knowledge of what disease is associated with ABCL dysfunction or what drugs/ligands affect a ABCL function. The members of the superfamily of ABC transporters are highly divergent in their effects and compound specificity. The utility of the claimed ABC transporter cannot be implicated solely from homology to known ABC transporters or their protein domains because the art does not provide a teaching stating that all members of the family of ABC transporters necessarily must have the same effects, have the same ligands or are involved in the same disease states. In fact, the art discloses evidence to the contrary. Appellants have used protein homology to predict the activity of the protein. The utility of the claimed ABC transporter cannot be implicated solely from homology to known ABC transporters or their protein domains because the art does not provide a teaching that all members of family of ABC transporter must have the same effects, the same ligands, and be involved in the same disease states.

Bork (Nature Genetics, Vol. 18, pages 313-318, 1998, see previous office action) provides a review disclosing the problems of using homology detection methods to assign function to related members of a family. Bork discloses: a) "While current homology detection methods can cope with data flow, the identification, verification and annotation of functional features need to be drastically improved" (page 313, column 1, Abstract), b) there are two bottle necks that need to be overcome en route to efficient functional predictions from protein sequences, i.e., "First, there is the lack of a widely accepted, robust and continuously updated suite of sequence analysis methods integrated into a

coherent and efficient prediction system. Second, there is considerable 'noise' in the presentation of experimental information, leading to insufficient or erroneous function assignment in sequence databases" (page 313, column 1, third paragraph), c) "In-depth analysis of protein sequences often results in functional predictions not attained in the original studies" (page 313, column 2, last paragraph), d) "---- more often than not, it is clear that the cellular role of the protein in question differs from that of the detected homologue(s) and there is currently no automatic means to establish how much functional information can be legitimately transferred by analogy from homologue to the query" (page 315, column 2, last paragraph), and e) pertaining to predictions of protein function, "do not simply transfer functional information from the best hit. The best hit is frequently hypothetical or poorly annotated; other hits with similar or even lower scores may be more informative; and even the best hit may have a different function". While "many proteins are multi functional, assignment of a single function, which is still common in genome projects, results in loss of information and outright errors". "It is typical that the general function of a protein can be identified easily but the prediction of substrate specificity is unwarranted; for example, many permeases of different specificity show approximately the same level of similarity to each other" (page 316). Karp (Bioinformatics, Vol 14, No.9, pages 753-754, 1998, see previous office action) has disclosed the problems of using functional prediction based on homology analysis. Karp states, a) "Although we know the accuracy with which sequence homologs can be determined, we know little about the accuracy of the overall process of assigning

function by homology (page 753, column 2, second paragraph), b) "We have more faith in the correctness of those sequences whose functions we determined experimentally, rather than through computational means (page 753, column 2, last paragraph), and c) "research is required to estimate the error rate of functional annotation by different methods of computational sequence analysis" (page 754, column 2, last paragraph). Bork (Current Opinion in Structural Biology, Vol 8, pages 331-332, 1998, see previous office action), discusses the problems with deriving biological knowledge from genomic sequences stating, "structural similarity does not lead to iron-clad functional predictions" (page 331, column 2 last paragraph), " does not necessarily mean a common evolutionary origin" (page 332, column 1, second paragraph), and "Today, what we predict from sequences is at best fragmentary and qualitative" (page 332, column 2, second paragraph). In summary the references discussed above disclose the unpredictability of assigning a function to a particular protein based on homology, especially one that belongs to the family ABC transporter which has very different ligand specificity and functions.

It can be argued the claimed ABC transporter protein is useful as a tool, as a reagent, and as a molecular target in the diagnosis and treatment of ABC transporter mediated disorders. All members of the ABC transporter protein family have a utility in selectively screening of candidate drugs that target ABC transporters. However, for a utility to be well-established it must be specific, substantial and credible. In this case all ABC transporters are in some combination useful in selective screening of candidate drugs that target ABC

transporter and in toxicology testing; however, the particulars of screening for candidate drugs that target the claimed ABC transporters, and in toxicology testing are not disclosed in the instant specification. None of the candidate drugs, toxic substances or the susceptible organ systems are identified. Therefore, this is a utility which would apply to virtually every member of a general class of materials, such as any collection of proteins or DNA. Because of this, such a utility is not specific and does not constitute a well-established utility. Further, because any potential diagnostic utility is not yet known and has not yet been disclosed, the utility is not substantial because it is not currently available in practical form. Moreover, use of the claimed protein for screening compounds that are a target for claimed ABC transporters protein is only useful in the sense that the information that is gained from the assay and is dependent on the effect it has on the protein, and says nothing with regard to each individual ABC transporter family. Again, this is a utility which would apply to virtually ever member of a general class of materials, such as any collection of proteins or DNA. Even if the expression of Applicants individual ABC transporter protein is affected by a test compound in an assay for drug screening, the specification does not disclose any specific and substantial interpretation for the result, and none is known in the art. Given this consideration, the instantly claimed method of using ABC transporter protein has no well-established use. The artisan is required to perform further experimentation on the claimed ABC transporter protein itself in order to determine to what use any information regarding this protein could be put.

With regard to diagnosis of disease, in order for a protein to be useful, as asserted, for diagnosis of a disease, there must be a well-established or disclosed correlation or relationship between the claimed ABC transporter protein and a disease or disorder. The presence of the claimed ABC transporter protein in tissue is not sufficient for establishing a utility in diagnosis of disease in the absence of some information regarding a correlative or causal relationship between the expression of the claimed ABC transporter protein and the disease. If a molecule is to be used as a surrogate for a disease state, some disease state must be identified in some way as associated with the molecule. There must be some expression pattern that would allow the claimed ABC transporter protein to be used in a diagnostic manner. Many proteins are expressed in normal tissues and diseased tissues. Therefore, one needs to know, e.g., that the claimed ABC transporter protein is either present only in, e.g. cancer tissue to the exclusion of normal tissue or is expressed in higher levels in diseased tissue compared to normal tissue (i.e. over expression). Evidence of a differential expression might serve as a basis for use of claimed ABC transporter protein as a diagnostic for a disease. However, in the absence of any disclosed relationship between the claimed ABC transporter protein and any disease or disorder and the lack of any correlation between the claimed ABC transporter protein with any known disease or disorder, any information obtained from an expression profile would only serve as the basis for further research on the observation itself. Congress intended that no patent be granted on a chemical compound whose sole utility consists of its potential role as an object of use-testing. *Brenner*, 148 USPQ at 696. The

disclosure does not present a substantial utility that would support the requirement of 35 U.S.C. 101.

Further, the ABC transporter family to which the polypeptide of SEQ ID NO:5 and 6 belong is a family in which the members have divergent functions. Although, ABC family members have the ability for ATP hydrolysis, assignment to this family does not support an inference of utility because the members are not known to transport the same compound. The ability to hydrolyze ATP provides energy for compound transport but discloses nothing about the substrate transported. There are some protein families for which assignment of a new protein in that family would convey a specific and utility to that protein. For example, some families of enzymes such as proteases, ligases, telomerases, etc. share activities due to the particular specific biochemical characteristics of the members of the protein family such as non-specific substrate requirements, that are reasonably imputed to isolated compositions of any member of the family. Without some common biological activity for the family members, a new member would not have a specific or substantial utility when relying only on the fact that it has structural similarity to the other family members. The members of the family have different biological activities, which may be related to tissue distribution but there is no evidence that the claimed compounds share any one of diverse number of activities. That is, no activity (i.e. substrate transported) is known to be common to all members. To argue that all the members can be used for drug screening, toxicology testing and diagnosis, is to argue a general, nonspecific utility that would apply to virtually every member of the family,

contrary to the evidence. Further, any compound could be considered as a regulator or modulator of tissue in that any compound, if administered in the proper amount, will stimulate or inhibit tissue. For example, salt, ethanol, and water are all compounds which will kill cells if administered in a great enough amount, and which would stimulate cells from which these compounds had been withheld, therefore, they could be considered regulators or modulators of tissue. However, use of these compounds for the modulation of tissue would not be considered a specific and substantial utility unless there was some disclosure of, for example, a specific and particular combination of compound/composition and application of such in some particular environment of use.

Without knowing a biological significance of the claimed ABC transporter protein, one of ordinary skill in the art would not know how to use the claimed invention in its currently available form in a credible real world manner based on the diversity of biological activities possessed by the ABC transporter family. Contrast *Brenner*, 148 USPQ at 694 (despite similarity with adjacent homologue, there was insufficient likelihood that the steroid would have similar tumor-inhibiting characteristics), with *In re Folkers*, 145 USPQ 390, 393 (CCPA 1965) (some uses can be immediately inferred from a recital of certain properties) or *In re Brana*, 34 USPQ 1436, 1441 (Fed. Cir. 1995) (evidence of success in structurally similar compounds is relevant in determining whether one skilled in the art would believe an asserted utility; here, an implicit assertion of a tumor target was sufficiently specific to satisfy the threshold utility requirement).

The assertion that the claimed invention has utility in drug screening, drug development and disease diagnosis, do not meet the standards for a specific, substantial or well-established utility for reasons set forth above. None of the utilities identified have been demonstrated to be specific to the polypeptide of SEQ ID NO:5 and 6 . One of ordinary skill in the art must understand how to achieve an immediate and practical benefit from the claimed species based on the knowledge of the class. However, no practical benefit has been shown for the use of the polypeptide SEQ ID NO:5 AND 6. Applicant has failed with respect to claimed ABC transporter protein, has not described the family of ABC transporter in enough detail to show, by a preponderance of the evidence, that the polypeptide of SEQ ID NO:5 AND 6 has any substantial use. The record shows that the family of ABC transporters is diverse, and has such a broad definition, that a common utility cannot be defined. Moreover, the evidence of record is inadequate to determine the disease(s), drug(s) or toxicological screen(s) for which the compounds would be useful. In *Brenner,* the Court approved a rejection for failure to disclose any utility for a compound where the compound was undergoing screening for possible tumor-inhibiting effects and an adjacent homologue of the compound had proven effective. *Brenner*, 148 USPQ at 690. Here, there is no evidence that the claimed isolated compounds have any utility.

For all the above reasons, the disclosure is insufficient to teach one of skill in the art how to use the invention.

The use of the claimed invention for toxicology testing, drug discovery, and disease diagnosis are not substantial utilities. The question at issue is whether or not the broad general assertion that the claimed ABC transporter protein might be used for some diagnostic application in the absence of a disclosure of which diagnostic application would be considered to be an assertion of a specific, substantial, and credible utility. For reasons set forth above the disclosure satisfies none of the three criteria *See In re Kirk*, 153 USPQ 48, 53 (CCPA 1967) (quoting the Board of Patent Appeals, □We do not believe that it was the intention of the statutes to require the Patent Office, the courts, or the public to play the sort of guessing game that might be involved if an applicant could satisfy the requirements of the statutes by indicating the usefulness of a claimed compound in terms of possible use so general as to be meaningless and then, after his research or that of his competitors has definitely ascertained an actual use for the compound, adducing evidence intended to show that a particular specific use would have been obvious to men skilled in the particular art to which this use relates)

The prior rejection under 101 followed *Brenner v. Manson*. In that case, the absence of a demonstrated specific utility for the claimed steroid compound was not ameliorated by the existence of a demonstrated general utility for the class. Unlike *Fujikawa v. Wattanasin*, where there were pharmaceutically acceptable in vitro results, here, there is nothing other than relatively low levels of sequence homology to a broad and diverse family of proteins having distinct modes of activity, and no disclosed common mode of action. A rejection under 112, first

paragraph, may be affirmed on the same basis as a lack of utility rejection under 101. *See, e.g., In re Swartz*, 56 USPQ2d 1703 (Fed. Cir. 2000); *In re Kirk*, 153 USPQ 48 (CCPA 1967.

4. Claims 19, 13-17, 38-43, 47 and 48 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention. Since neither the specification nor the art of record disclose any activities or properties that would constitute a real world context of use for the claimed ABC transporter (SEQ ID NO:5 and 6) further experimentation is necessary to attribute a utility to the claimed ABC transporter. Specifically, since the claimed invention is not supported by either a specific or substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art would not know how to use the claimed invention so that it would operate as intended without undue experimentation.

The claims fail to disclose how to use the claimed invention for the reasons given above (lack of utility). Further the claims are drawn to an orphan ABC transporter polypeptide whose activity, activating ligands and functionality have not been disclosed. Neither the claims nor the specification disclose what specific biological activity is associated with the claimed ABC transporter polypeptide. There is no disclosure of the specific compounds that are transported, proteins activated in the signal transduction pathway or what ligand

is capable of binding to the claimed polypeptide. Therefore unrelated and inactive proteins are encompassed by the claims. The specification does not disclose how to produce active variants or how to use inactive ones. Substitutions, additions or deletion that result in active variants are not disclosed. Substitutions additions or deletion that are detrimental to claimed ABC transporter variant activity are not disclosed. There is no disclosure of how to assay variants since the ligand and function of the claimed invention is unknown.

The complex nature of ABC transporter activity (disclosed above) and the unpredictability of assigning a function to claimed transporter with no known ligand, activity, or function is described in the rejection under 35 USC 101 and 35 USC 112, 1st paragraph.

Specifically, since the claimed invention is not supported by either a specific or substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art would not know how to use the claimed invention so that it would operate as intended without undue experimentation.

The activity of the ABC transporter is unknown. Polypeptides encoded by polynucleotides that would hybridize to the polynucleotide of SEQ ID NO:4 encompass unrelated and inactive variants. Polypeptides encoded by polynucleotides that would hybridize to the polynucleotide encoding the polypeptide of SEQ ID NO:5 encompass unrelated and inactive variants. Applicant has not disclosed how to use unrelated and inactive variants. Applicant has not disclosed how to isolate or make functional variants

encompassing the limitations of the claimed invention. Instant fact pattern closely resembles that in Ex parte Maizel, 27 USPQ2d 1662 (BPAI 1992). In Ex parte Maizel, the claimed invention was directed to compounds, which were defined in terms of function rather than sequence (i.e., "biologically functional equivalents"). The disclosed compound in both the instant case and in Ex parte Maizel was the full length, naturally occurring protein. The claimed compounds in instant application are polypeptides isolated using polynucleotides that hybridize to a particular polynucleotide. The critical feature of the invention as it relates structure to function is not required to be contained in the hybridizing sequence. In Ex parte Maizel the Board found that there was no reasonable correlation between the scope of exclusive right desired by Appellant and the scope of enablement set forth in the patent application. Even though Appellant in Ex parte Maizel urged that the biologically functional equivalents would consist of proteins having amino acid substitutions wherein the substituted amino acids have similar hydrophobicity and charge characteristics such that the substitutions are "conservative" and do not modify the basic functional equivalents of the protein, the Board found that the specification did not support such a definition, and that the claims encompassed an unduly broad number of compounds. Such is the instant situation. Clearly, a single disclosed sequence does not support claims to any polypeptide encoded by a nucleic acid isolated by the hybridization, given the lack of guidance regarding what sequences would hybridize specifically to the polynucleotide of SEQ ID NO:4 and sequence complementary thereto, and not hybridize to other, unrelated sequences. Further, many of the polypeptides

encoded by the nucleic acids isolated will be unrelated to the protein of SEQ ID NO:5, being devoid of its characteristic structural and functional features. The specification does not disclose how to use the unrelated compounds isolated by claimed method. Further, many compounds isolated may be inactive. The specification does not disclose how to use inactive compounds. Inactive compounds may be truncated polynucleotides devoid of function and lacking the critical feature that relates structure to function. Due to the large quantity of experimentation necessary to identify the polypeptides with the structural and functional features of instant invention, the lack of direction/guidance presented in the specification regarding the identification, purification, isolation and characterization of said polynucleotides and polypeptides, the unpredictability of the effects of mutation on the structure and function of proteins and nucleic acids (since mutations of SEQ ID NO:4 and 5 are also encompassed by the claim), and the breadth of the claim which fail to recite meaningful structural and functional limitations, undue experimentation would be required of the skilled artisan to make or use the claimed invention in its full scope.

Further claim 9 encompasses every polypeptide known and unknown to man. Applicant has not disclosed how to isolate all the proteins encompassed by the claim or to assay for their activity. Applicant has not disclosed how to use all the proteins encompassed by the claims.

As is evidence in the discussions *supra*, undue experimentation would be required by the skilled artisan to make and use the instant invention.

8. Claims 9, 14, 15, 16,17, 38-39, 41-43 are rejected under 35 U.S.C. 1 12, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant that the inventors, at the time the application was filed, had possession of the claimed invention.

Applicants argue the specification explicitly teaches the amino acid sequence for murine and human ABCL polypeptide (Figures 1 and 2), the specification inherently discloses fragments of murine and human ABCL polypeptide, since fragments are merely portions of the specifically disclosed full-length murine and human ABCL polypeptide sequences. Further, Applicants argue they have disclosed an exemplary embodiment of an ortholog of the polypeptide of SEQ ID N0: 5 (human) in Example 3 where the murine ortholog of SEQ ID NO:5 is cloned, isolated, and sequenced. Applicants further argue they provide detailed description f how one of skill can determine percentage identity of a sequence with the sequence of SEQ ID N0: 5, and how amino acid sequences biological function can be identified in an amino acid sequence using various analysis software, Applicants contend that in view of the explicitly-disclosed sequences provided by the instant application, one of ordinary skill in the art could readily determine the structure of amino acid molecules that are fragments of the polypeptide of SEQ ID N0: 5 or the polypeptide encoded by the DNA insert of ATCC Deposit No. PTA-3111, and would recognize that Applicants

were in possession of the claimed invention. Applicants, therefore, submit that the claims satisfy the written description requirement of 35 U.S.C. 112, first paragraph, and request reconsideration and withdrawal of this rejection.

Applicant's arguments have been fully considered but are not found persuasive. The claims are drawn to polypeptide variants of the protein disclosed in SEQ ID NO:5, said variants may be unrelated, structurally and functionally, to the protein encoded by SEQ ID NO:5 . The common function of the polypeptide of SEQ ID NO:5, which is based upon a common property or critical technical feature of the genus claimed is not disclosed. The claims, as written, encompass polypeptides which vary substantially in length and also in amino acid composition. The instant disclosure the polypeptide of SEQ ID NO:5 does not adequately describe the scope of the use of the claimed genus, which encompasses a substantial variety of subgenera including proteins, polypeptides, derivatives, allelic variants, chimeric constructs, fusion constructs, fragments, variants etc. The claims also encompass polypeptides with at least about 70% identity to SEQ ID NO:5 and fragments of SEQ ID NO:5. The claims also encompass polypeptides that can be completely different from the polypeptide of SEQ ID NO:5, e.g. in claim 9p, the whole molecule can be changed by insertions, deletions etc. there are many problems with the claims for example, the claims require that a) polypeptide possess an activity but the activity is not disclosed, or b) polypeptide possess no specific activity. Essentially the claims are drawn to a genus pf polypeptides that is defined only by sequence identity because no

activity that relates structure to function is disclosed. The specification has not disclosed a single substation that can be made to retain activity.

To provide evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of compete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof. In this case, the only factor present in the claim is a partial structure in the form of a recitation of percent identity. There is no identification of any particular portion of the structure of the polypeptide of SEQ ID No:5 that must be conserved for activity. Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description of the claimed genus.

Naming a type of material generically known to exist, in the absence of knowledge as to what that material consists of, is not a description of that material. When one is unable to envision the detailed constitution of a complex chemical compound having a particular function, such as a protein or nucleic acid, so as to distinguish it from other materials, as well as a method for obtaining it, conception has not been achieved until reduction to practice has occurred, i.e., until after the protein or nucleic acid has been isolated. Thus, claiming all proteins or DNAs that achieve a result without defining what means will do so is not in compliance with the description requirement. Rather, it is an attempt to preempt the future before it has arrived. The claims recite a broad

arbitrary structural relationship between the claimed polypeptide sequence and the single disclosed species of amino acid sequence. The claims are not even directed to a polypeptide with a particular functional activity. Therefore, non-functional or functionally unrelated proteins to ABCL are encompassed by the claims. The recited structural relationships are arbitrary since neither the specification nor the prior art discloses any definitive relationship between protein function and % identity or homology at either the nucleotide or amino acid level; and the specification does not describe a single species of functional protein that is not 100% identical to the recited amino acid sequence.

While one of skill in the art can readily envision numerable species of amino acid sequences that are at least a given % identity to a reference polypeptide sequence, one cannot envision which of these also encode a polypeptide with a specific activity of the protein of SEQ ID NO:5 and 6. The fact remains that the actual protein, with a particular activity, or the actual amino acid sequences of such a protein *cannot* be envisioned any better when the possible choices are narrowed from all possible sequences to all possible sequences with an arbitrary structural relationship with a known functional less sequence. For example, if one skilled in the art were to make a synthetic polypeptide sequence with 90% identity to the reference amino acid sequence, he would be no more able to say whether it was a functional polypeptide belonging to the claimed genus than a polypeptide that was only 10% identical to the reference polypeptide sequence. Nor would he be able to say whether the sequence existed in nature.

To put the situation in perspective, the number of possible amino acid sequences of 100 amino acids in length is 20^{100} (approx. 10^{130}). The number of possible amino acid sequences that are of a given %identity relative to a reference sequence, where all differences between the possible sequences and the reference sequence are substitutions, can be calculated by the following formula:

$$N = XL + X^2L(L-1)/2! + X^3L(L-1)(L-2)/3! + \ldots + X^{n-1}L(L-1)(L-2)\ldots(L-(n-2))/(n-1)! + X^nL(L-1)(L-2)\ldots(L-(n-1))/n!$$

where N is the number of possible sequences, X is the number of different residues that can be substituted for a residue in the reference sequence, L is the length of the reference sequence, n is the maximum number of residues that can be inserted, deleted or substituted relative to the reference sequence at a given % identity. For an amino acid sequence, X is 19 (alternate amino acids).

For a 100 amino acid sequence that is at least 90% identical to a reference sequence of 100 amino acids, the number of possible sequences having 9 amino acid substitutions relative to the reference (the penultimate term of the formula) is approximately 6×10^{23}. Whereas the number of possible sequences having 10 amino acid substitutions relative to the reference (the final term of the formula) is approximately 1.1×10^{26}. So the last term is approximately equal to N, i.e. the preceding terms contribute little to the total. It can also be shown that N can be approximated by the formula $X^nL^n/n!$, where $n<<L$. Using this formula to approximate N in this example gives a value of 1.7×10^{26}.

In the present case, the reference amino acid sequence, SEQ ID NO 5, is 2146 amino acids long. Using the approximation formula, the number of possible amino acid sequences that are at least e.g. 70% identical to the reference amino acid would be much larger than 6×10^{23}. While limiting the scope of potential sequences to those that are at least e.g. 70% identical to a reference greatly reduces the number of potential sequences to test, it does not do so in any meaningful way. All of these values greatly exceed the estimated number of atoms in the universe (10^{70} to 10^{90}). Thus, limiting the claims by the recited structural relationships merely reduces the degree of impossibility of making and testing sequences for those which are functional proteins encompassed by the claims. Therefore, inclusion of the structural relationships in the claim does not distinguish the instant fact situation from those reviewed in *Amgen, Fiers,* and *Regents of the Univ. Calif.*

The specification does not provide any information on what amino acid residues are necessary and sufficient for a functional activity. The specification also provides no teachings on what amino acid sequence modifications, e.g. insertions, deletions and substitutions, would be permissible in an active ABCL polypeptide that would improve or at least would not interfere with the biological activity or structural features necessary for the biological activity and stability of the protein. Since there are no other examples of proteins that have structural homology with SEQ ID NO:5 and a defined activity, it is not possible to even guess at the amino acid residues which are critical to its structure or function based on sequence conservation. Therefore one cannot predict variant amino

acid sequences for a biologically active polypeptide. Rather one must engage in case to case painstaking experimental study to determine active ABCL variants. Consequently, excessive trial and error experimentation would have been required to identify the necessary nucleic acid sequence derivatives encoding a biologically active ABCL with an amino acid sequence differing from SEQ ID NO:5 since the amino acid sequence of such polypeptides could not be predicted.

The specification discloses only one putative amino acid sequences, SEQ ID NO:5, for a polypeptide having the necessary properties for the disclosed uses, and provides no guidance on obtaining functional polypeptide variants of SEQ ID NO:18 encoded by SEQ ID NO:17 which would be suitable.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111 , clearly states that applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description" inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the ad to recognize that (he or she) invented what is claimed." (See *Vas-Cath* at page 1116). As discussed above, the skilled artisan cannot envision the detailed chemical structure of the encompassed genus of polynucleotides, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is

required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

One cannot describe what one has not conceived. See *Fiddes v. Baird,* 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF'S were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

There is no disclosure of the compound transported by the claimed genus polypeptides. The claimed polypeptide is essentially is an orphan transporter whose activity, associated function and activating ligands have not been disclosed. The neither specification nor prior art provide a specific assay for the genus claimed. Polypeptides comprising variants of ABCL may be completely unrelated to the protein of SEQ ID NO:5 or polypeptide of SEQ ID NO:6 The complexity of assigning a function and membership into a the genus of proteins is highlighted by Bork and Karp (discussed above), who disclose assigning function by homology is unpredictable by using the complete sequence of an protein, let alone using variants which may not have any domains related to a particular function. Neither the claims nor the specification disclose what specific biological activity is associated with the claimed polypeptide or the special technical feature encompassed by specific domains associated with a specific activity of the claimed genus. The superfamily of transporters are specialized proteins designed for chemical recognition of ligands, transport of specific compounds, and subsequent transduction of information encoded in those ligands/compounds to the machinery of the cell. Transporters interact with

many diverse compounds having diverse effects. The important features which would help to define the ABCL activity and define the genus claimed have not been disclosed in the specification nor prior art. Further the activity transduced is not disclosed or how it relates structure to function.

The claims encompass nucleic acids encoding proteins which are structurally and functionally unrelated to the protein of SEQ ID NO:5. Therefore instant specification fails to provide sufficient descriptive information, such as definitive structural/ functional features of the claimed genus of polypeptides/polynucleotides. There is no description of the conserved regions which are critical to the structure and function of the genus claimed. The neither specification nor claims disclose the specific activity of the orphan ABCL of instant invention, how it is assayed, nor a description of the conserved regions which are critical to the structure and function of the genus claimed. Further allelic variants, derivatives, orthologs, splice variants, fragments comprising undefined amino acids lacking a critical structural feature of the invention composition comprising claimed ABCL polypeptide are also rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. It is also noted that the gene encoding the ABCL has not been isolated, therefore Applicants were not in possession of allelic variants or splice variants. There is no disclosure of intron/exon structure

of gene or alleles claimed. Not a single mutation was constructed which contained a defined activity allowing transport of a specific substrate.

Therefore, only isolated polypeptide comprising the amino acid sequence set forth in SEQ ID NO: 5 and 6 but not the full breadth of the claims meets the written description provision of 35 U.S.C. 112, first paragraph. Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 U.S.C. 112 is severable from its enablement provision (see page 1 115).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

9. Claims 9, 15, 16, 17, 38-39 and 41 rejected under 35 U.S.C. 102(b) as being anticipated by Luciani, R. et al, Database PIR-79, Accession No. A54774, April 5, 1995, see previous office action).

.Luciani discloses a polypeptide which has 49.6% query match and 49.6% identity to the polypeptide of SEQ ID NO:5. The polypeptide disclosed by Luciani

is a) fragment comprising at least about 25 amino acid residues SEQ ID NO: 5, wherein the fragment is antigenic; b) a polypeptide with the amino acid sequence as set forth in SEQ ID NO: 5 with at least one modification selected from the group consisting of amino acid substitutions, amino acid insertions, amino acid deletions, C-terminal truncation, and N-terminal truncation, c) the derivative of the polypeptide set forth in any of SEQ ID NO: 5. Further the polypeptide disclosed by Luciani is classified as an ABC transporter and therefore has the activity of an ABC transporter.

Therefore the limitations of claims 9, 15, 16, 17 38-39 and 41 are met by the disclosure of Luciani, absent evidence to the contrary.

11. Claims 9, 14, 15, 16,17, and 41 rejected under 35 U.S.C. 102(e) as being anticipated by Hayden. et al, US Patent 6,617,122, see previous office action).

Hayden discloses a polypeptide (SEQ ID NO:1) which has 51.8% query match and 50.3% identity to the polypeptide of SEQ ID NO:5. The polypeptide disclosed by Hayden is a) fragment comprising at least about 25 amino acid residues SEQ ID NO: 5, wherein the fragment is antigenic; b) a polypeptide with the amino acid sequence as set forth in SEQ ID NO: 5 with at least one modification selected from the group consisting of amino acid substitutions, amino acid insertions, amino acid deletions, C-terminal truncation, and N-terminal truncation, c) the derivative of the polypeptide set forth in any of SEQ ID NO: 5. Further the polypeptide disclosed by Hayden is classified as an ABC transporter and therefore has the activity of an ABC transporter. Also Hayden

discloses compositions of the polypeptide may contain pharmaceutically acceptable formulation agents (carrier, adjuvant, solubilizer, stabilizer or anti-oxidant) such as water, saline, polyethylene glycols such as polyethylene glycol (column 40). Therefore the limitations of claims 9, 14, 15, 16,17, 38, 39 and 41 are met by the disclosure of Hayden, absent evidence to the contrary.

12. No claim is allowed.

13. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nirmal S. Basi whose telephone number is 571-272-0868. The examiner can normally be reached on 9:00 AM-5:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Janet Andres can be reached on 571-272-0867. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

NSB

Nirmal S. Basi
Art Unit 1646
4/14/06

JANET L. ANDRES
SUPERVISORY PATENT EXAMINER